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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/330,215	06/11/1999	ROBERTO PORTA	108907-09014	9134

7590

09/17/2002

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT PAPER NUMBER

1615

DATE MAILED: 09/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/330,215

Applicant(s)

Porta

Examiner

Gollamudi Kishore

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jul 17, 2002
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 and 19-22 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 and 19-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

The requests for refund and reconsideration dated 7-17-02 are acknowledged.

Claims included in the prosecution are 1-12 and 19-22.

Claim Rejections - 35 U.S.C. § 103

- 1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:**

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

- 2. Claims 1-12 and 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over applicant's statements of prior art in combination with Litzinger (BBA, 1996) of record by itself or in further combination with Maccarone (BBRC, 1992), Eastman (Human Gene Therapy, 1997) individually or in combination. Applicant indicates on pages 3-7 of the specification that instant polynucleotides are known for their function.**

Litzinger while disclosing formulations containing cationic liposomes and their complexes with polynucleotides teaches that oligonucleotides have the inability to efficiently traverse through cellular membranes and hence complexation with cationic liposomes (note the abstract and page 140).

Maccarone teaches that DNA when complexed with cationic liposomes are able to transfect protoplasts (note the abstract).

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Similarly, Eastman teaches that the complex prepared by the addition of cationic liposomes and DNA has an efficient transfection ability (note the abstract and Materials and methods).

The use of cationic liposomes for the delivery of art known polynucleotides would have been obvious to one of ordinary skill in the art in view of Litzinger's teachings that oligonucleotides do not have the ability to cross cellular membrane, but are able to efficiently transfect when complexed with cationic liposomes as also shown by Maccarone and Eastman.

Applicant's arguments have been fully considered, but are not found to be persuasive. It would appear that applicant's arguments are once again based on the definition of the term, transfection. Applicant submits 'Pharmaceutique OMS reference argue that this reference shows that Defibrotide does not have mutagenic potential in the bacterial system and therefore, does not possess transfection capability. This argument is not found to be persuasive and a similar argument based on transfection has already been addressed by the examiner in the previous action. To summarize, :- though the classical definition of transfection pertains to genetic material, this term is known to be used for the transfer of therapeutic molecules besides nucleic acids to a recipient. The examiner has already cited the reference of Lee (5,908,777) in this context (see abstract and col. 3, line 20-27 for instance). Therefore, whether claimed polydeoxyribonucleotides have the classical transfection ability is not the issue. The issue here is whether the cationic liposomes taught

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by the prior art are able to deliver, as vectors, the claimed art known polydeoxyribonucleotides to the intended donors and the prior art clearly shows the ability of the cationic liposomes to perform this function, irrespective of their intended function. Furthermore, instant claim 1 does not recite Difibrotide.

With regard to Lee, applicant point out col. 1, lines 56-60 of Lee and argue that Lee teaches that cationic liposome- DNA complexes are unstable. This argument is not found to be persuasive since Lee's statement is a general statement as background to his invention and Lee does not provide any experimental data. Secondly, the references used in the rejection, that is, the references of Litzinger, Maccarone and Eastman do not teach or suggest any instability. In fact, as pointed out in the earlier action and as admitted by applicant himself, Zelphati teaches that cationic liposomes are able to protect oligonucleotides from nuclease digestion. Stability of oligonucleotides is logical since nucleases cannot digest them. In response, applicant argues that Zelphati discloses simply a general property of complexes of cationic liposomes with oligonucleotides once delivered to the cells and the stability is by protection against nucleases present inside the cells. This argument is not found to be persuasive since the statements on page 34 by Zelphati includes the in vitro studies in cell culture medium and human serum. If the cationic liposome-oligonucleotide complexes are stable in this hostile environment, it is reasonable for one of ordinary skill in the art to expect the complexes to be stable in an aqueous buffer

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environment since no factors which cause the instability are present in the aqueous system.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.



Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

September 16, 2002